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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN FRANCISCO DIVISION

GUARDANT HEALTH , INC.

Plaintiff and Counterclaim-Defendant,

vs.

NATERA, INC.

Defendant and Counterclaim-Plaintiff.

Case No. 3:21-cv-04062-EMC

DEFENDANT NATERA'S ANSWER TO COMPLAINT AND COUNTERCLAIMS

Defendant Natera, Inc. ("Natera"), by and through its undersigned counsel, hereby files its Answer, Affirmative Defenses, and Counterclaims to Plaintiff Guardant Health Inc.'s ("Guardant") Original Complaint. Natera demands a trial by jury on all issues so triable. Natera denies any allegation in the Complaint that is not specifically admitted. Natera has re-produced the Complaint's section headings for ease of reference; to the extent any headings or subheadings in the Complaint make factual allegations that would require a response if stated in the main text, Natera denies all such allegations and claims for relief. Natera responds to each paragraph in the Complaint as follows:

I. INTRODUCTION

1. This case concerns Plaintiffs Guardant Reveal™ ("Reveal") liquid biopsy cancer assay for early-stage colorectal cancer (CRC) patients, and Defendant Natera's campaign of false and misleading advertising directed at this important and innovative diagnostic product. As the world's leading provider of comprehensive circulating tumor DNA (ctDNA) assays for clinical use, Guardant's oncology platform—including its gold-standard Guardant360®, Guardant360® CDx, and GuardantOMNI® assays—have helped improve clinical outcomes, while lowering healthcare costs, for advanced stage cancer patients around the world.

ANSWER: Natera denies the allegations in Paragraph 1 of the Complaint.

2. Leveraging its patented technology, vast data sets, and advanced analytics, Guardant recently launched Reveal, a plasma-only liquid biopsy test that detects residual and recurrent CRC in about 7 days from a simple blood draw. For oncologists, Reveal improves the management of early-stage CRC patients by detecting ctDNA in plasma after surgery, enabling doctors to identify patients with residual CRC who may benefit from post-surgery chemotherapy (adjuvant chemotherapy), months earlier than current standard-of-care tests permit. Reveal is the first test for minimal residual disease (MRD) detection that detects ctDNA in the plasma of CRC patients following treatment ***without the need for a tissue sample and sequencing*** to determine the particular mutations that were present in the patient's tumor. Reveal achieves outstanding sensitivity

(91%) for predicting recurrence of CRC disease.

ANSWER: Natera admits that Guardant launched Reveal, a plasma-only liquid (tumor-naïve) biopsy test, in or around February 2021. Except as expressly admitted, Natera denies the allegations in Paragraph 2 of the Complaint.

3. With little or no concern for the CRC patients who could be harmed, Natera has undertaken a campaign of misinformation to convince customers and potential customers, including oncologists and other physicians, cancer researchers, health care institutions, biopharmaceutical companies, and genetic laboratories, to avoid using Reveal in favor of Natera's own Signatera™ ("Signatera"), a tumor-dependent assay. In its commercial advertising and promotion, Natera makes literally false and misleading statements that disparage Guardant's new assay, and falsely asserts that Signatera is superior to Reveal across a variety of metrics, including sensitivity,[1] failure rate,[2] negative predictive value (NPV),[3] and Hazard Ratio,[4] among other categories. These claims are false. Natera combines outright misrepresentations with scientifically unfounded comparisons based on cherry-picked metrics, data artifacts, and noncomparable clinical studies to exaggerate the purported benefits of Signatera while inaccurately denigrating Reveal. In truth, Reveal has important clinical advantages over Signatera—including its superior landmark sensitivity, its availability for patients from whom tumor samples are unavailable, and its faster initial turnaround time from sample collection to assay results—all of which Natera ignores.

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[1] "Sensitivity" refers to the assay's ability to identify which patients will develop recurrences based on MRD detection by ctDNA assay. A higher percentage indicates a test is more sensitive.

[2] "Failure rate" refers to the percentage of time a ctDNA assay fails to provide a result at all, whether positive or negative. For any test, a lower failure rate is more desirable.

[3] "NPV" refers to the assay's ability to correctly predict which patients will subsequently not develop a recurrence of CRC (i.e., a "negative" test result means CRC will not recur).

[4] The "Hazard Ratio" refers to a comparison between the recurrence rate over time in CRC patients who tested positive for MRD by ctDNA assay, to the recurrence rate in CRC patients who tested negative for MRD by ctDNA. A larger hazard ratio suggests that the assay is potentially more useful in successfully distinguishing CRC patients whose cancers will or will not recur.

ANSWER: Natera denies the allegations in Paragraph 3 of the Complaint.

4. Guardant seeks to enjoin Natera from continuing to make or disseminate false and misleading statements about the performance of Reveal and Signatera; to require Natera to retract, remove, and correct these false and misleading advertising claims; and to recover damages and other relief for the harm that Natera has inflicted on Guardant.

ANSWER: Natera admits that Guardant has filed a complaint in this action purporting to seek injunctive relief against Natera but denies that Guardant is entitled to any relief. Except as expressly admitted, Natera denies the allegations in Paragraph 4 of the Complaint.

II. PARTIES

5. Plaintiff Guardant is a Delaware corporation having its principal place of business at 505 Penobscot Dr., Redwood City, California 94063.

ANSWER: Natera admits the allegations in Paragraph 5 of the Complaint.

6. Guardant was founded in 2012 by pioneers in DNA sequencing and cancer diagnostics. Since its inception, Guardant has focused its expertise on the development of liquid biopsy assays for cancer. It was the first company to develop and commercialize a comprehensive liquid biopsy assay to identify genomic biomarkers for advanced solid tumors using cell-free ctDNA, from simple, non-invasive blood draws.

ANSWER: Natera admits that Guardant was founded in 2012. Except as expressly admitted, Natera denies the allegations in Paragraph 6 of the Complaint.

7. Today, Guardant is a leading precision oncology company focused on helping conquer cancer globally through the use of its proprietary blood tests, vast data sets, and advanced

analytics. The Guardant oncology platform leverages its capabilities to drive commercial adoption, improve patient clinical outcomes, and lower healthcare costs across all stages of the cancer care continuum. Guardant Health has commercially launched the liquid biopsy-based Guardant360®, Guardant360® CDx, and GuardantOMNI® tests for advanced stage cancer patients, and recently launched its Reveal test for early-stage CRC patients.

ANSWER: Natera admits that Guardant launched the liquid biopsy-based Guardant360®, Guardant360® CDx, and GuardantOMNI® tests for advanced stage cancer patients and that it launched the Reveal test in or around February 2021. Except as expressly admitted, Natera denies the allegations in Paragraph 7 of the Complaint.

8. Defendant Natera is a Delaware corporation having its principal place of business at 13011 McCallen Pass, Building A, Suite 100 Austin, Texas 78753, and offices at 201 Industrial Rd., San Carlos, California 94070. Natera may be served with process by serving a copy of this Complaint on its Registered Agent: National Registered Agents, Inc., 1209 Orange Street, Wilmington, Delaware 19801.

ANSWER: Natera admits the allegations in Paragraph 8 of the Complaint.

9. Natera markets and sells Signatera, a product it describes as a "personalized, tumor-informed assay optimized to detect circulating tumor DNA (ctDNA) for molecular residual disease (MRD) assessment and recurrence monitoring for patients previously diagnosed with cancer." Signatera competes with Reveal in the market for ctDNA assays that can be used after surgery on CRC patients, to detect recurrences and evaluate the need for adjuvant chemotherapy.

ANSWER: Natera admits the allegations in Paragraph 9 of the Complaint.

III. JURISDICTION AND VENUE

10. This is an action for false advertising under Section 43(a) of the Lanham Act, 15 U.S.C. § 1125(a); for false advertising in violation of Cal. Bus. & Prof. Code § 17500 et seq.; for unlawful trade practices in violation of Cal. Bus. & Prof. Code § 17200 et seq.; and for unfair competition in violation of the common law of California and other states in which Defendant is conducting its activities.

ANSWER: Natera admits that Guardant has filed a complaint purporting to assert claims asserted claims against Natera. Natera states that the complaint speaks for itself, and no response is required. Natera denies that any of Guardant's claims against Natera are valid. To the extent an answer is required, Natera denies the allegations in Paragraph 10 of the Complaint.

11. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331 and 1338 and 15 U.S.C. §§ 1051, et seq.

ANSWER: The allegations in Paragraph 11 of the Complaint state legal conclusions that Natera is neither required to admit nor deny.

12. This Court has jurisdiction over Plaintiff's state law claims pursuant to 28 U.S.C. § 1367 and the doctrine of supplemental jurisdiction.

ANSWER: The allegations in Paragraph 12 of the Complaint state legal conclusions that Natera is neither required to admit nor deny.

13. The exercise of personal jurisdiction in California is proper both because of Defendant's ongoing and systematic contact with California and the Northern District of California, including its maintenance of a regular place of business in the District, and because acts giving rise to Plaintiffs causes of action have occurred in the Northern District of California. Specifically,

Natera markets, promotes, advertises, offers for sale, sells, and/or distributes Signatera to customers including oncologists and other physicians, cancer researchers, health care institutions, biopharmaceutical companies, genetic laboratories, and/or others throughout the United States, including in the Northern District of California. Defendant has purposefully and voluntarily placed Signatera into the stream of commerce with the expectation that this product will be purchased by customers in the Northern District of California. Furthermore, Natera falsely and misleadingly advertises Signatera to customers, including oncologists, pathologists, additional physicians, health care institutions, pharmaceutical companies, and/or others throughout the United States, including in the Northern District of California.

ANSWER: The allegations in Paragraph 13 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. To the extent an answer is required, Natera admits that Natera markets, promotes, advertises, offers for sale, sells, and/or distributes Signatera to customers including oncologists and other physicians, cancer researchers, health care institutions, biopharmaceutical companies, genetic laboratories, and/or others throughout the United States, including in the Northern District of California. Except as expressly admitted, Natera denies the allegations in Paragraph 13 of the Complaint.

14. Venue is proper in the Northern District of California pursuant to 28 U.S.C. § 1391.

ANSWER: The allegations in Paragraph 14 of the Complaint state legal conclusions that Natera is neither required to admit nor deny.

IV. FACTUAL BACKGROUND

A. Early Identification of At-Risk Patients is a Key to Preventing Recurrence of Colorectal Cancer and Prolonging Survival

15. Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the second leading cause of cancer death in the United States in both men and women. While a majority

of patients are diagnosed with early-stage disease, nearly a third of patients whose CRC spreads into adjacent tissues and lymph nodes will die from their disease within five years.

ANSWER: Natera admits the allegations in Paragraph 15 of the Complaint.

16. Surgery alone is often curative for early-stage CRC, and in later-stage cases, adjuvant chemotherapy after surgery can reduce the risk of recurrence. However, clinicians have had very limited means of identifying patients that require adjuvant chemotherapy. Thus, the development of effective clinical tests to identify CRC patients with MRD—i.e., a small number of CRC cells remaining in the body that can later multiply and cause recurrence of the disease— after surgery has long been recognized as a need, to help doctors both identify patients who may benefit from additional therapy, and avoid administering unnecessary and toxic treatment to patients who will not benefit from it.

ANSWER: Natera denies that clinicians have had very limited means of identifying patients that require adjuvant chemotherapy since the clinical launch of Signatera, in 2019. Natera admits the remaining allegations in Paragraph 16 of the Complaint.

17. Because residual cancer cells that remain in the body following treatment typically cause no physical signs or symptoms and are present at very low levels that are undetectable with standard techniques, detecting and monitoring MRD has required development of advanced and highly sophisticated technologies with the requisite precision and sensitivity for clinical decision-making. Reveal provides that sophisticated technology.

ANSWER: Natera admits the allegations in the first sentence of Paragraph 17 of the Complaint. Natera denies the remaining allegations in Paragraph 17 of the Complaint.

B. Liquid Biopsy Technology Allows Assessment of MRD by Detecting Circulating Tumor DNA in Blood

18. Human blood contains fragments of DNA that are shed into the bloodstream by dying cells in tissues—including cancers. Such fragments derived from tumor cells are known as circulating tumor DNA (ctDNA). This phenomenon led to the development of so-called "liquid biopsies" a game-changing technology capable of detecting the presence of cancer in patients by detecting ctDNA in their blood, and eventually led to liquid biopsies specifically designed to assess MRD following treatment of CRC. Liquid biopsies using simple blood draws offer major advantages for identifying MRD, because they are quick, convenient, and minimally invasive, and can be easily repeated to monitor for the presence of ctDNA over time.

ANSWER: Natera admits the allegations in the first two sentences of Paragraph 18 of the Complaint. Natera denies the remaining allegations in Paragraph 18 of the Complaint.

19. However, detecting and characterizing the very low concentrations of ctDNA present in the blood of patients with MRD, and using that information to stratify CRC patients as high- or low-risk for recurrence, requires an assay that is both highly sensitive and specific. Recognizing this need, Guardant expended substantial resources and time to develop Reveal, a clinical blood-based assay to evaluate ctDNA in blood using advanced DNA sequencing methods. Launched in February 2021, Reveal is the first commercially available plasma-only ctDNA assay, capable of detecting MRD in post-operative CRC patients without the need for prior sampling and sequencing of tumor tissue or the time needed to create a new, customized test for each new patient.

ANSWER: Natera admits the allegations in the first sentence of Paragraph 19 of the Complaint. Natera also admits that Reveal launched in or around February 2021. Except as expressly admitted, Natera denies the remaining allegations in Paragraph 19 of the Complaint.

20. Most important, Reveal ***works.*** Peer-reviewed data published by Parikh et al. in the

journal Clinical Cancer Research shows that Reveal offers 91% recurrence sensitivity (i.e., ability to identify which patients will recur based on ctDNA detection) and 100% positive predictive value[5] for recurrence (i.e., all patients Reveal identified as having a "positive" ctDNA test result later recurred).

ANSWER: Natera denies the allegations in Paragraph 20 of the Complaint.

21. Natera offers a liquid biopsy MRD assay it calls Signatera, which it launched commercially in 2019. Natera advertises, promotes, markets, and sells Signatera to oncologists and other physicians, cancer researchers, health care institutions, biopharmaceutical companies, genetic laboratories, and others nationwide, including in California. Unlike Reveal, Signatera is a "tumor-informed" (tumor-dependent) assay. It requires initial genomic profiling of tumor tissue taken from the individual patient. Information from the tumor tissue is then used to identify a panel of tumor-derived mutations specific to that patient, which then can be monitored through testing of blood samples collected throughout the patient's disease course.

ANSWER: Natera admits that Natera launched Signatera clinically in 2019. Except as expressly admitted, Natera denies the remaining allegations in the first sentence of Paragraph 21. Natera admits the allegations in second-through-fifth sentences of Paragraph 21 of the Complaint.

22. Tumor-dependent assays like Signatera have meaningful drawbacks. Specifically, a significant number of CRC patients—particularly those treated with chemotherapy prior to surgery—may not have sufficient samples of tumor tissue to allow initial genomic profiling of the tumor. For these patients, a plasma-only ctDNA assay like Reveal provides the ***only*** option for MRD detection using ctDNA. Furthermore, acquiring sufficient tissue specimens can be painful,

[5] Positive predictive value (PPV) refers to the assay's ability to correctly predict which patients will subsequently develop a recurrence of CRC (i.e., "positive" test result means CRC will recur).

dangerous, time consuming and create significant delays in MRD testing turnaround time. Reveal reduces the time spent waiting for results needed to decide whether high-risk patients require adjuvant chemotherapy from approximately three weeks to 7 days. For patients with a potentially lethal disease, this reduction in wait time is critical for both outcomes (earlier initiation of chemotherapy has been associated with improved outcomes) and for peace of mind.

ANSWER: Natera denies the allegations in Paragraph 22 of the Complaint.

C. Natera's Advertising Falsely Claims that Signatera is Superior to Reveal, and that Reveal is Unproven and Insensitive

23. Fearful that Signatera cannot compete with Reveal and Guardant on the merits, Natera falsely and misleadingly advertises and promotes Signatera in comparison to Reveal. In its advertising, Natera deceptively characterizes Reveal as unproven, insensitive, and consequently and unfoundedly "detrimental to patients," while touting Signatera's supposed superiority.

ANSWER: Natera denies the allegations in Paragraph 23 of the Complaint.

24. Natera's advertising is based on irrelevant metrics, misrepresented data artifacts, and misleading and inapt comparisons, presented in disregard of the actual scientific evidence supporting Reveal's substantial benefits for oncologists and their patients. Carefully timed to coincide with the very launch of Reveal, Natera's false and misleading comparisons of Reveal and Signatera have harmed Guardant, and will continue to cause Guardant irreparable harm if not stopped.

ANSWER: Natera denies the allegations in Paragraph 24 of the Complaint.

1. Natera's Advertising Falsely Claims Signatera Is Superior to Reveal

25. Shortly after Reveal's commercial launch in February 2021, Natera began contacting

both its and Guardant's current and potential customers, including leading cancer centers like the Mayo Clinic, expressing supposed "concern" about "other laboratories rushing into the clinical MRD market and making potentially misleading claims" that Natera asserted "may be detrimental to patients." In a "Dear Colleague" advertisement dated March 2, 2021, which, on information and belief, Natera widely emailed to both its and Guardant's customers and potential customers, Natera stated:

> Natera is committed to the science and precision of molecular residual disease (MRD) testing for improving patient care. We are proud that Signatera data has been published or presented from over 2,000 patients across 30+ tumor histologies. As this exciting field gains momentum, especially in early-stage CRC, there is concern about other laboratories rushing into the clinical MRD market and making potentially misleading claims with no peer-reviewed evidence, which may be detrimental to patients. As you review the evidence for any new MRD test, please keep in mind several minimum requirements for MRD product performance and clinical validation

(emphasis in original).

ANSWER: Natera admits that the block quote in Paragraph 25 is an accurate quotation from an email sent by Natera on or around March 2, 2021. Natera asserts that the excerpt is only a select portion of the referenced document, and that the document speaks for itself and is the best source of its full content and context. Natera denies the allegations in Paragraph 25 of the Complaint to the extent they do not accurately represent the document's full content and context. Except as expressly admitted, Natera denies the allegations in Paragraph 25 of the Complaint.

26. In the same promotional email, Natera sent these customers and potential customers

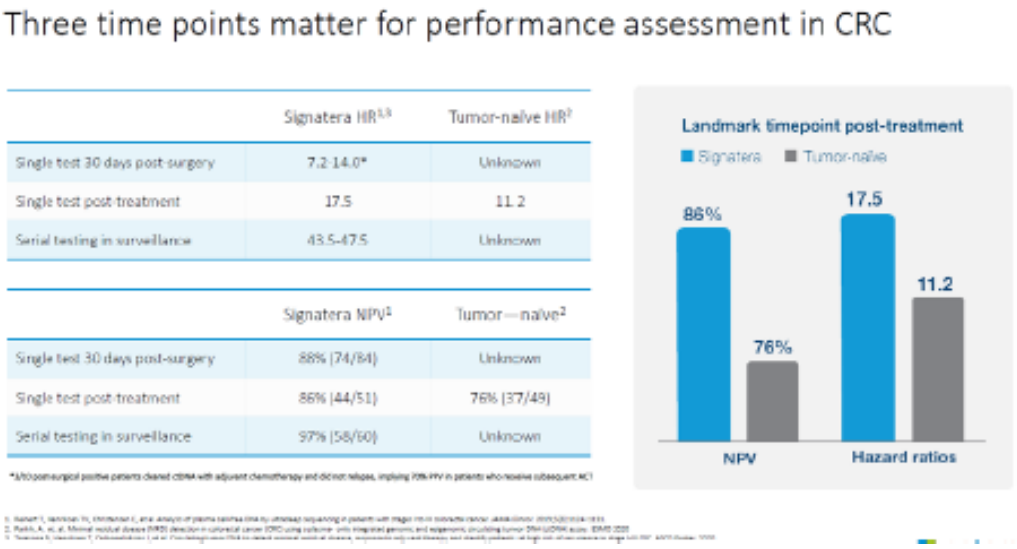
a slide presentation entitled "Evidence Review: Tumor-informed vs. tumor-naive MRD." Though not identifying Reveal by name, Natera's presentation expressly references data presented by "Parikh, A. et al." at the 2020 European Society for Medical Oncology (ESMO) conference—a study specifically concerning Reveal. Moreover, Reveal is the ***only*** "tumor-naive" (that is, plasma-only) ctDNA assay for detecting MRD in CRC patients available on the market, and is also the only ctDNA assay for MRD introduced at or around the time Natera sent this presentation.

ANSWER: Natera denies that Reveal is the only tumor-naïve ctDNA assay for detecting MRD in CRC patients. Natera admits the remaining allegations in Paragraph 26 of the Complaint.

27. Natera's "Evidence Review" falsely criticizes "tumor-naive methods," that is, Reveal, as unsupported by "peer-reviewed evidence." In fact, interim data from the very study cited by Natera—Parikh et al.—was peer-reviewed before being published, first as abstract- presentations at three separate prestigious scientific meetings (ASCO 2019, ESMO 2019, and ESMO 2020), and later as an article in the April 29, 2021 issue of the journal Clinical Cancer Research.

ANSWER: Natera denies the allegations in Paragraph 27 of the Complaint.

28. Natera further erroneously claims that, while Signatera's "test performance" is "unsurpassed," Reveal is not only inferior to Signatera, but has "unknown" performance with respect to sensitivity and hazard ratios for two of three "time points" that "matter":



ANSWER: Natera admits that its March 2021 document entitled "Evidence Review: Tumor-informed vs. tumor-naive MRD" states on the second page: "Test performance with tumor-informed method is unsurpassed." Natera further admits that the image contained in Paragraph 29 is an excerpt from the sixth page of the same March 2021 document. Natera asserts that these excerpts are only select portions the referenced document, and that the document speaks for itself and is the best source of its full content and context. Natera denies the allegations in Paragraph 25 of the Complaint to the extent they do not accurately represent the document's full content and context. states that the document referenced in Paragraph 28 of the Complaint speaks for itself. To the extent Paragraph 28 contains factual allegations requiring a response, Natera denies the allegations in Paragraph 28 of the Complaint.

29. These statements too are false, as explained below. But rather than correcting its falsehoods, Natera repeated and amplified them—repeatedly.

ANSWER: Natera denies the allegations in Paragraph 29 of the Complaint.

30. Shortly after Natera distributed its "Evidence Review," Parikh et al.'s previously presented data supporting the clinical performance of Reveal, derived from plasma specimens from 84 CRC patients undergoing curative intent surgery, was published in the peer-reviewed journal Clinical Cancer Research. Nonetheless, Natera renewed and repeated its previous criticisms of Reveal on its website, including in a broadly misleading "white paper to learn how our tumor-informed approach stacks up against a tumor naive assay" found at https://www.natera.com/wp-content/uploads/2021/05/SGN_WP_Solar_20210503_NAT-9000052_FINAL_DWNLD.pdf.

ANSWER: Natera admits that the Parikh study was first published in the journal *Clinical Cancer Research* on or around April 29, 2021. Natera also admits that it published a document entitled "A comparison of tumor-informed and tumor-naive approaches for early-stage molecular residual disease (MRD) detection" at the hyperlink contained in Paragraph 30 of the Complaint. Except as expressly admitted, Natera denies the allegations in Paragraph 30 of the Complaint.

31. In its white paper, which Natera publishes on its website to influence customers and potential customers to purchase Signatera rather than Reveal, Natera purports to compare "Signatera (tumor informed assay)" to a "Tumor-naive assay," that is, plasma-only Reveal, citing data that appear to show—again, falsely—that Reveal is "not validated," or that Signatera significantly outperforms Reveal on every referenced metric, including "Hazard ratios" and "Negative predictive value (NPV)":

Table 3. *Comparison of hazard ratios and negative predictive values of tumor-informed and tumor-naive assays in early-stage CRC*

	Signatera (tumor-informed assay)[4,7,8]	Tumor-naive assay[10]
Hazard ratios of ctDNA (positive vs negative)		
Post-surgery (30 day single test)	7.2-14.0*	Not Validated
Post-ACT (single test)	17.5	9.8-11.2**
Serial testing	43.5-47.5	11.4
Negative predictive value (NPV)		
Post-surgery (30 day single test)	88% (74/84)	Not Validated
Post-ACT (single test)	86% (44/51)	76% (37/49)**
Serial testing	97% (58/60)	82% (41/50)

ANSWER: Natera admits that the image in Paragraph 31 is an excerpt from the document published on Natera's website, at https://www.natera.com/wp-content/uploads/2021/05/SGN_WP_Solar_20210503_NAT-9000052_FINAL_DWNLD.pdf and that the excerpted image reflects information about hazard ratios and NPV for Signatera and tumor-naïve assays. Natera asserts that the excerpt is only a select portion of the referenced document, and that the document speaks for itself and is the best source of its full content and context. Natera denies the allegations in Paragraph 31 of the Complaint to the extent they do not accurately represent the document's full content and context. Except as expressly admitted, Natera denies the allegations in Paragraph 31 of the Complaint.

32. Natera's white paper further asserts that: "Without the genomic information for each primary tumor, tumor naive assays are unable to filter out background biological noise from CHIP or to avoid tracking driver mutations that may be subjected to selection pressure from treatment . . . ,"[6] But this is false; Reveal can and does filter out CHIP background noise bioinformatically. In fact, data publicly presented in 2018 on a prototype of the Reveal assay showed 100% specificity with incorporation of the CHIP filter.

Signatera vs. Reveal performance comparison

	Signatera	Reveal
Validation data published or presented (# patients analyzed)	> 2,000[1,2]	< 150[4,5]
Pre-surgical sensitivity in CRC	89-94%[1,3]	47%[4]
Failure rate in CRC – tissue and plasma combined	< 3%[3]	12-14%[4]
Number of blood tubes required	2	4
Diagnostic lead time vs. radiographic recurrence in CRC (avg)	8.7 months[1]	~4 months[4]
Post-surgical NPV/PPV in CRC (30 days post-surgery)	88% / 100%[*1]	not reported[6]
Serial longitudinal NPV in CRC	97%[1]	82%[4]
Serial longitudinal Hazard Ratio in CRC	43.5[1]	11.4[4]
Serial longitudinal sensitivity in CRC	88-94%[1,2]	69%[4]
Quantitation of ctDNA burden for monitoring purposes	Tumor copies per mL	none

ANSWER: Natera states that the document referenced in Paragraph 32 speaks for itself. To the extent Paragraph 32 contains factual allegations requiring a response, Natera denies the allegations in Paragraph 32 of the Complaint.

33. In May 2021, Natera also published on its public-facing website advertising entitled "Investor presentation," which purports to compare "Signatera vs. Reveal performance":

ANSWER: Natera admits that it posted an investor presentation on its website in May 2021 and that the heading of Slide No. 12 of such presentation is entitled "Signatera vs. Reveal performance comparison. Except as expressly admitted, Natera denies the allegations in Paragraph 33 of the Complaint.

[6] "CHIP" refers to clonal hematopoiesis of indeterminate potential—mutations from blood cells that can lead to false positive results when testing for MRD.

34. Shortly after posting the May 2021 performance comparison on its website, Natera began disseminating it—repeatedly—to the same customers and potential customers in order to tout Signatera's supposed superiority over Reveal.

ANSWER: Natera denies the allegations in Paragraph 34 of the Complaint.

35. Similar to its "Evidence Review" and white paper advertising, Natera's May 2021 performance comparison claims to demonstrate quantitatively that Signatera is superior to Reveal across a wide-ranging set of metrics. Here, these metrics purportedly include "pre- surgical sensitivity," "failure rate," "diagnostic lead time," [7] "post-surgical" and "serial longitudinal" negative predictive value (NPV), and "Hazard Ratio," among other categories. All of this is false and misleading.

ANSWER: Natera admits that Slide 12 of an investor presentation Natera published in May 2021 references data regarding pre-surgical sensitivity, failure rate, diagnostic lead time, post-surgical negative predictive value, hazard ratio, and other categories, for both Signatera and Reveal. Except as expressly admitted, Natera denies the allegations in Paragraph 35 of the Complaint.

2. Natera's Advertising is False and Misleading

36. In reality, each of Natera's promotional claims of superiority, including the express and implied claims contained in its "Evidence Review," white paper, and the "Signatera vs. Reveal performance comparison" are false and misleading. They also either deceived or are likely to deceive oncologists and other physicians, cancer researchers, health care institutions, biopharmaceutical companies, and genetic laboratories, and other customers and potential customers into believing that Reveal is untested, inaccurate, insensitive, and inferior to Signatera.

[7] "Diagnostic lead time" refers to the time between the first MRD detection by ctDNA assay and the first confirmation of CRC recurrence by standard radiographic imaging methods. A longer diagnostic lead time is generally observed with higher sensitivity tests.

ANSWER: Natera denies the allegations in Paragraph 36 of the Complaint.

37. Any valid comparison between diagnostic tests, including ctDNA assays for detecting MRD in CRC patients—and specifically including Signatera and Reveal—must be supported by properly designed, head-to-head studies that directly compare the two assays using the same test procedures and protocols in the same patient population. Cross-test comparisons, especially where the purpose and methodology of the underlying studies differ significantly, and/or where the studies are conducted in different patient populations, necessarily lead to a misleading apples-to-oranges result that cannot legitimately be used to claim that one test is superior to the other.

ANSWER: Natera denies the allegations in Paragraph 37 of the Complaint.

38. To date, no such head-to-head studies involving Signatera and Reveal and using the same test protocol and study population are available. Instead, Natera's purported comparisons of the "performance" of Signatera vs. Reveal largely rely on data published by Parikh et al. concerning Reveal, and data published by Reinert et al. for Signatera. These different studies used very different test protocols and analysis methods, and examined very different patient populations. Consequently, Natera's claims of superiority based on these improper comparisons are false, misleading, and deceptive.

ANSWER: Natera admits that it is not aware of any direct head-to-head studies involving Signatera and Reveal as described in Paragraph 38. Except as expressly admitted, Natera denies the allegations in Paragraph 38 of the Complaint.

39. In fact, many of Natera's cherry-picked comparison metrics are unrelated to assay "performance" at all. While Natera touts the number of "patients analyzed" in "published or presented studies," which Natera claims is more than two thousand for Signatera, those numbers do

not prove the superiority of the clinical ***performance*** of one ctDNA assay over another. Moreover, the ">2,000" number reported for Signatera is inflated. It double-counts some patients whose data were used in more than one published study, and it includes patient populations presenting with cancers other than CRC for which Reveal is neither validated nor intended to be used.

ANSWER: Natera denies the allegations in Paragraph 39 of the Complaint.

40. Likewise, Natera claims that Signatera requires only two "blood tubes," while Reveal requires four. But again, this is not a "performance" metric at all. But even there, Natera's representation that Reveal "requires" 4 tubes is false. Reveal, like Signatera, only requires 2 tubes of blood. Unlike Natera, Guardant's Reveal kit collects 2 additional tubes of blood to provide redundancy in the rare event of an assay failure on the first 2 blood tubes; thereby protecting patients from having to provide another blood sample and saving valuable time.

ANSWER: Natera admits that Signatera only requires two tubes of blood. Except as expressly admitted, Natera denies the allegations in Paragraph 40 of the Complaint.

41. Finally, "quantitation of ctDNA for monitoring purposes" is an assay ***feature,*** not an appropriate measure of assay ***performance.*** Natera's assertions that quantitation, i.e., "quantitative results," is necessary to achieve good assay performance, or is an "MRD assay requirement," are misleading. This is particularly so in light of the intended use of both the Signatera and Reveal assays: to identify CRC patients at increased risk for recurrence of the disease. All available evidence shows that the presence of ctDNA—regardless of the quantity— indicates a high likelihood of recurrence. As such, the clinical utility of ctDNA quantitation in the context of the intended use of the assay is unclear, at best. Natera's assertion that "quantitation is essential for monitoring tumor response during the patient's treatment," is unsupported by any studies showing that an improvement in patient outcome is achieved by knowing or acting on changes in ctDNA quantity during treatment. Because it is wholly unsupported, Natera's claim is false. Signatera's

practice of reporting a "mean tumor molecules per mL" value, and Reveal's choice not to do so, does not represent a performance advantage for one over the other.

ANSWER: Natera denies the allegations in Paragraph 41 of the Complaint.

42. While these false and misleading claims are harmful, it is Natera's misrepresentations concerning Reveal's actual performance metrics that are the most damaging to Guardant and its new assay.

ANSWER: Natera denies the allegations in Paragraph 42 of the Complaint.

43. **Failure rate:** Natera's comparison of "failure rate in CRC," and its claim of Signatera's superiority over Reveal, are false. As the article published by Parikh et al. in the April 29, 2021 issue of Clinical Cancer Research states, this study—which Natera cites as proof that Reveal has a "12-14%" failure rate (vs. a "< 3%" rate for Signatera)—relied on ***banked*** plasma or cell free DNA samples that had input amounts substantially less than recommended. Indeed, as Parikh et al. stated explicitly in the cited publication, "the extracted ctDNA quantity or quality was below the recommended and optimal input levels for the assay" and "may have affected overall performance characteristics." In point of fact, the actual failure rate of Reveal in patient care testing is ***less than 1%,*** better than Signatera's claimed failure rate of less than 3%.

ANSWER: Natera admits that the third sentence contains two accurate quotations from the Parikh et al. study. Natera asserts that the quotations are only isolated excerpts of the referenced document, and that the document speaks for itself and is the best source of its full content and context. Natera denies the allegations in Paragraph 43 of the Complaint to the extent they do not accurately represent the document's full content and context. Except as expressly admitted, Natera denies the allegations in Paragraph 43 of the Complaint.

44. **Pre-surgical sensitivity:** Natera's claims of Signatera's superior "pre-surgical sensitivity" ("89-94%" vs. "47%") is functionally meaningless and highly misleading. Reveal is not intended or indicated to be used as a diagnostic tool pre-surgery. And, as an assay that relies on the existence of surgically-excised tumor tissue, Signatera ***cannot*** be used as a pre-surgical diagnostic tool (meaning it has a real-world pre-surgical clinical sensitivity of 0%). Moreover, the study Natera cites as the source of this statistic—Parikh et al.—contains a population where nearly half (45%) of the study cohort had received chemotherapy prior to surgery and in which the pre-surgical sample volumes were far lower than recommended. Such pre-surgical treatment suppresses ctDNA, and thus necessarily lowers the ctDNA detection rate and low sample volume also can affect assay sensitivity.

ANSWER: Natera admits that the Parikh et. al study reported that 45% of patients received neoadjuvant therapy. Except as expressly admitted, Natera denies the allegations in Paragraph 44 of the Complaint.

45. **Post-surgical NPV/PPV:** Natera's further comparison of the 30-day post- surgical negative and positive predictive value (NPV/PPV) for Signatera vs. Reveal, (i.e., 88%/100% vs. "not reported" or "not validated"), is similarly misleading. For many CRC patients, surgery to remove the tumor does not represent the end of the patient's initial treatment regimen; many patients receive adjuvant chemotherapy. While—contrary to Natera's claim— Parikh et al. ***did*** report data that could be used to calculate a 30-day post-surgical NPV and PPV for Reveal, they ***did not*** focus on—nor did they draw conclusions from—data from this timepoint. The 30-day post-surgical MRD timepoint is relevant for clinical MRD testing to assist with adjuvant therapy decisions during patient care. It is not the appropriate timepoint in an observational/retrospective research study to validate certain performance metrics, like PPV or NPV, of assays like Signatera or Reveal that are intended to predict disease recurrence.

ANSWER: Natera denies the allegations in Paragraph 45 of the Complaint.

46. Simply put, adjuvant therapy works, and can cure MRD-positive patients that otherwise would have recurred. As such, estimates of an assay's NPV and PPV, when sourced from samples collected after surgery but before adjuvant chemotherapy, are confounded by the effect of chemotherapy and are uninterpretable—one cannot sort out the merits of the assay from the effects of the chemotherapy. Parikh et al. purposely chose to report data from samples collected after all definitive treatment to avoid this confounding factor precisely because nearly 55% of the study participants received additional treatment post-surgery.

ANSWER: Natera admits that adjuvant therapy is sometimes effective to cure MRD-positive patients that otherwise would have recurred. Except as expressly admitted, Natera denies the allegations in Paragraph 46 of the Complaint.

47. Meanwhile, other assay performance metrics, such as sensitivity to detect recurrence are not subject to the confounding effect of post-operative chemotherapy. Nor is sensitivity to detect recurrence subject to the confounding effects of the baseline population risk, as described below. Thus sensitivity would be a more appropriate metric to compare assay performance at the 30-day post-surgery timepoint than NPV. However, Natera chose not to report this metric in its marketing materials, presumably because it shows Signatera's performance is ***less*** favorable compared to Reveal. As reported by Reinert et al., the sensitivity of Signatera to detect recurrence using the 30-day post-surgical timepoint is 7/17 patients (41%). This metric as reported by Parikh et al. in the supplemental data shows 14/26 patients (54%). Among the subset of patients with stage I-III disease (excluding stage IV patients, a more similar stage representation to the Reinert et al. data), the Reveal data still show an even higher sensitivity for recurrence of 9/16 (56%).

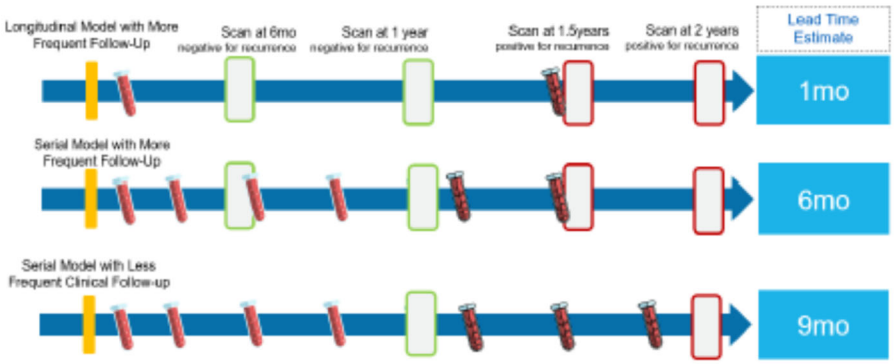
ANSWER: Natera denies the allegations in Paragraph 47 of the Complaint.

48. In short, PPV as a metric of assay validity must be taken from samples collected after

all therapy is complete and where sufficient follow-up is available. Underscoring the importance of this—and the misleading nature of the values presented by Natera's advertising— the PPV for both assays is 100% when these conditions are met.

ANSWER: Natera denies the allegations in Paragraph 48 of the Complaint.

49. **Diagnostic lead time:** Natera's unfavorable comparison of Reveal's "diagnostic lead time vs. radiographic recurrence," to that of Signatera, is also false and misleading. The calculation of a "diagnostic lead time estimate" is affected as much by the frequency of the tests that are used to derive the estimate as it is by the assay's sensitivity. As the following graphic shows, the diagnostic lead time estimate for the ***same assay and the same patient with same test results*** can vary significantly, depending on how often follow-up testing is conducted.



ANSWER: Natera denies the allegations in Paragraph 49 of the Complaint.

50. Because Natera's diagnostic lead time estimates are derived from studies having different protocols and testing regimens, its comparison is fundamentally flawed and unreliable. The "diagnostic lead time estimate" for Signatera was developed from data reported by Reinert et al. Reinert's study protocol called for CRC patients to undergo ctDNA testing 30 days after surgery, and every three months afterwards, for three years or until the patient's death or withdrawal from

the study. In contrast, the study by Parikh et al. did not involve patient testing at regular intervals over a specified period of time and was not designed to estimate "diagnostic lead time." Consequently, Parikh et al. did not report an estimated diagnostic lead time for Reveal, and the 4 months" value Natera fabricated for Reveal has no reliable basis in fact.

ANSWER: Natera admits the allegations in the second and third sentences of Paragraph 50. Except as expressly admitted, Natera denies the allegations in Paragraph 50 of the Complaint.

51. **"Serial longitudinal" NPV, hazard ratio, and sensitivity:** Likewise, Natera's comparisons of the "serial longitudinal" NPV, hazard ratio, and sensitivity of Signatera and Reveal are fundamentally misleading. Parikh et al.'s study of Reveal was not designed to provide "serial" test data (i.e. testing at regular time intervals after the initial test), and consequently did not report these statistics. Natera nevertheless biased its comparison with Reveal in Signatera's favor by reporting Parikh et al.'s "***longitudinal***" sensitivity of 69%, which is calculated in patients who had at least one surveillance draw, the timing of which was highly variable relative to the time of recurrence, and is in no way similar to the timing of sample collection employed by Reinert et al. This is fundamentally a misleading apples-to-oranges comparison. However, the Parikh et al. study includes a subset of recurrence positive patients who had a Reveal sample available within 4 months of recurrence. Using these data to estimate the ***"serial*** longitudinal" sensitivity parameter, Reveal has an estimated sensitivity of 91%-comparable (or superior) to Signatera. Despite the valid estimate of 91% being clearly outlined in the Parikh et al. paper, Natera chose to use a fabricated and invalid "longitudinal" sensitivity estimate, again presumably because it cast Reveal in a less favorable light.

ANSWER: Natera admits that the Parikh et al. study reported a "longitudinal sensitivity" of 69% for Reveal. Except as expressly admitted, Natera denies the allegations in Paragraph 51 of the Complaint.

52. Beyond its choice to disregard differences in testing frequency, Natera further biased its serial longitudinal NPV and hazard ratio comparisons by ignoring the significant differences in the patient populations from which the data were drawn. The Reinert et al. study using Signatera examined patients with stages I to III CRC, where the CRC recurrence rate was 19% (24/125 evaluable patients). In contrast, the patients included in the Parikh et al. study were more than twice as likely to recur (39%, 27/70 evaluable patients) demonstrating that the patients in this study had a much higher risk of disease recurrence than those studied by Reinert et al. Assays of equal sensitivity and specificity yield dramatically different NPVs and hazard ratios when applied to patient populations with different risk profiles. Natera's deliberate failure to account for this difference results in false and highly deceptive comparisons.

ANSWER: Natera admits the allegations in the second sentence of Paragraph 52. Natera denies the remaining allegations in Paragraph 52 of the Complaint.

D. Natera's False and Misleading Advertising Has Caused or Will Likely Cause Harm to Patients and to Guardant

53. Natera's commercial advertising and promotions have had their intended effect. Natera's efforts to disparage the performance of Reveal while falsely touting Signatera has misled or is likely to mislead oncologists, healthcare institutions, and other potential customers, and caused these customers to order Signatera rather than Reveal for their CRC patients.

ANSWER: Natera denies the allegations in Paragraph 53 of the Complaint.

54. In addition, Natera's false statements regarding Reveal have injured, or are likely to injure, the reputation of this product and the reputation of Guardant itself, costing Guardant customer good will and causing the loss of future sales. Natera's express and necessarily implied assertions that Reveal has "significant gaps in study design and performance," and is less sensitive and predictive than Signatera, sow doubt among oncologists and others about the utility and

performance of Reveal. Natera explicitly reinforces this doubt by warning doctors that using Reveal may "be detrimental to patients." Natera's assertions will cause, and on information and belief may have already caused, some CRC patients to lose opportunities for rapid MRD detection and the attendant benefits of timely guided treatment decisions. They are also likely to cause irreparable harm to Guardant's business and reputation.

ANSWER: Natera denies the allegations in Paragraph 54 of the Complaint.

55. By misleading oncologists and other medical professionals into believing that Reveal is unsupported, insensitive and inferior to Signatera, Natera has caused patients to miss the benefits of Guardant's validated and effective plasma only liquid biopsy assay.

ANSWER: Natera denies the allegations in Paragraph 55 of the Complaint.

COUNT I:

FALSE ADVERTISING IN VIOLATION OF

SECTION 43(a)(1)(B) OF THE LANHAM ACT, 15 U.S.C. § 1125(a)(1)(B)

56. Plaintiff repeats and hereby realleges the allegations above as if fully set forth herein.

ANSWER: Natera repeats its answers to the allegations above as if fully set forth herein.

57. In its commercial advertising and promotion to potential customers, Defendant markets Signatera by stating and implying that Reveal suffers from significant gaps in study design and performance, and that Signatera's performance is superior to Reveal.

ANSWER: Natera denies the allegations in Paragraph 57 of the Complaint.

58. Defendant's promotional claims about the relative clinical support and performance of Reveal and Signatera are false and/or misleading. The data Defendant relies upon to draw its comparisons in favor of Signatera are derived from studies conducted by different researchers, employing different methodologies and procedures, using different patient populations, and having different qualities and characteristics that do not permit a fair or valid comparison. Defendant disregards data that show Reveal has excellent clinical performance.

ANSWER: Natera denies the allegations in Paragraph 58 of the Complaint.

59. These claims violate Section 43(a) of the Lanham Act, which provides in relevant part that a "person who, or in connection with any goods or services . . . uses in commerce any . . . false or misleading description of fact or misleading representation of fact, which ... in commercial advertising or promotion, misrepresents the nature, characteristics, qualities, or geographic origin of his or her or another person's goods, services, or commercial activities, shall be liable to a civil action by any person who believes that he or she is likely to be damaged by such act."

ANSWER: The allegations in Paragraph 59 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. To the extent an answer is required, Natera denies the allegations in Paragraph 59 of the Complaint. Natera specifically denies that it has violated the Lanham Act or any other federal or state law.

60. Defendant's promotional claims about the performance of Reveal, alone and in comparison to Signatera, are material. The clinical characteristics and performance of cancer diagnostic procedures are of paramount importance to doctors responsible for treating patients with life-threatening illnesses like CRC.

ANSWER: The allegations in Paragraph 60 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. To the extent an answer is required, Natera denies

the allegations in Paragraph 60 of the Complaint.

61. Pursuant to 15 U.S.C. § 1117, Plaintiff is entitled to damages for Defendant's Lanham Act violations, an accounting of profits made by Defendant on sales of its product, as well as recovery of the costs of this action.

ANSWER: The allegations in Paragraph 61 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. To the extent an answer is required, Natera denies the allegations in Paragraph 61 of the Complaint. Natera specifically denies that Guardant is entitled to damages, an accounting of profits allegedly made by Natera on sales of its product, recovery of the costs of this action, or any other relief.

62. Defendant's acts are willful, wanton and calculated to deceive, and are undertaken in bad faith, making this an exceptional case entitling Plaintiff to recover reasonable attorneys' fees pursuant to 15 U.S.C. § 1117.

ANSWER: The allegations in Paragraph 62 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. To the extent an answer is required, Natera denies the allegations in Paragraph 62 of the Complaint. Natera specifically denies that Guardant is entitled to attorneys' fees or any other relief.

63. Unless enjoined by this Court, Defendant's acts will irreparably injure Plaintiffs goodwill and erode its market share. Pursuant to 15 U.S.C. § 1116, Plaintiff is entitled to preliminary and permanent injunctive relief to prevent Defendant's continuing acts.

ANSWER: The allegations in Paragraph 63 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. To the extent an answer is required, Natera denies the allegations in Paragraph 63 of the Complaint. Natera specifically denies that Guardant is entitled

to any form of injunctive relief or other relief.

COUNT II:

FALSE ADVERTISING IN VIOLATION OF

CAL. BUS. & PROF. CODE § 17500 ET SEQ.

64. Plaintiff repeats and hereby realleges the allegations above as if fully set forth herein.

ANSWER: Natera repeats its answers to the allegations above as if fully set forth herein.

65. Plaintiff brings this cause of action pursuant to CAL BUS. & PROF. CODE § 17535 in an individual capacity and not on behalf of the general public.

ANSWER: Natera states that the Complaint speaks for itself, and no response is required to the allegations in Paragraph 65. Natera specifically denies all liability under the California Business and Professions Code, or any other state or federal law.

66. CAL. BUS. & PROF. CODE § 17500 provides that it is unlawful for any person, firm, corporation, or association to dispose of property or perform services, or to induce the public to enter into any obligation relating thereto, through the use of untrue or misleading statements.

ANSWER: The allegations in Paragraph 66 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. Natera further states that Guardant purports to describe a statute that speaks for itself. To the extent an answer is required, Natera denies the allegations in Paragraph 66 of the Complaint.

67. Cal. Bus. & Prof. Code § 17508 provides:

> It shall be unlawful for any person doing business in California and advertising to consumers in California to make any false or misleading advertising claim, including claims that (1) purport to be based on factual, objective, or clinical evidence, that (2) compare the product's effectiveness or safety to that of other brands or products, or that (3) purport to be based on any fact.

ANSWER: To the extent any response is required, Natera admits that Guardant purports to quote from Cal. Bus. & Prof. Code § 17508, a statute which speaks for itself. Natera denies that it has violated any provision of the California Business & Professions Code or any other state or federal statute.

68. Defendant's misleading statements violate CAL. BUS. & PROF. CODE §§ 17500 and 17508, and Plaintiff has acted in response to and reliance on the misleading statements made by Defendant regarding the performance of Signatera and Reveal, including by expending time, money, and other resources on preparing its sales force to respond to these misleading statements.

ANSWER: The allegations in Paragraph 68 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. To the extent an answer is required, Natera denies the allegations in Paragraph 68 of the Complaint. Natera specifically denies that it has violated Cal. Bus. & Prof. Code §§ 17500 or 17508, or any other state or federal law.

69. Defendant's conduct has caused Plaintiff damage in an amount to be determined at the trial herein but not less than $75,000 and, unless enjoined by this Court, Defendant's conduct will continue to cause Plaintiff irreparable damage for which Plaintiff has no adequate remedy at law.

ANSWER: The allegations in Paragraph 69 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. To the extent an answer is required, Natera denies the allegations in Paragraph 69 of the Complaint. Natera specifically denies that it has caused

Guardant any damage.

70. Pursuant to CAL. BUS. & PROF. CODE § 17535, Plaintiff seeks an order of this Court compelling the Defendant to provide restitution, and to disgorge the monies to which Plaintiff is entitled but were instead collected and realized by Defendant as a result of its false and misleading statements and injunctive relief enjoining Defendant from making such false and misleading statements.

ANSWER: Natera states that the Complaint speaks for itself. To the extent an answer is required, Natera denies the allegations in Paragraph 70 of the Complaint. Natera specifically denies any liability to Guardant, whether in law or equity.

COUNT III:
UNLAWFUL TRADE PRACTICE IN VIOLATION OF CAL. BUS. & PROF. CODE § 17200 *ET SEQ.*

71. Plaintiff repeats and hereby realleges the allegations above as if fully set forth herein.

ANSWER: Natera repeats its answers to the allegations above as if fully set forth herein.

72. Pursuant to CAL. BUS. & PROF. CODE § 17200, unfair competition is "any unlawful, unfair or fraudulent business act or practice and unfair, deceptive, untrue or misleading advertising . . . ." The misleading statements made by Defendant regarding the performance of Signatera in comparison to Plaintiffs Reveal violate CAL. BUS. & PROF. CODE § 17200 et. seq. Moreover, Defendant's conduct constitutes a violation of the Lanham Act, and thus as unlawful business conduct is separately actionable as a violation of CAL. BUS. & PROF. CODE § 17200 et. seq. Defendant's conduct is also otherwise unfair and therefore a violation of these provisions.

ANSWER: The allegations in Paragraph 72 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. To the extent an answer is required, Natera denies the allegations in Paragraph 72 of the Complaint. Natera specifically denies that Natera has violated any provision of the California Business & Professions Code, the Lanham Act, or any other state or federal law.

73. Defendant's conduct has caused Plaintiff damage in an amount to be determined at the trial herein, and, unless enjoined by this Court, Defendant's conduct will continue to cause Plaintiff irreparable damage for which Plaintiff has no adequate remedy at law.

ANSWER: The allegations in Paragraph 73 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. To the extent an answer is required, Natera denies the allegations in Paragraph 73 of the Complaint. Natera specifically denies that it has caused damage to Guardant.

74. Pursuant to CAL. BUS. & PROF. CODE § 17203, Plaintiff seeks an order of this Court compelling the Defendant to provide restitution, and to disgorge the monies to which Plaintiff is entitled but were instead collected and realized by Defendant as a result of its false and misleading statements and injunctive relief enjoining Defendant from making such false and misleading statements.

ANSWER: The allegations in Paragraph 74 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. To the extent an answer is required, Natera denies the allegations in Paragraph 74 of the Complaint. Natera specifically denies any liability to Guardant, whether in law or equity.

COUNT IV:

COMMON LAW UNFAIR COMPETITION

75. Plaintiff repeats and hereby realleges the allegations above as if fully set forth herein.

ANSWER: Natera repeats its answers to the allegations above as if fully set forth herein.

76. With full knowledge of Plaintiff's Reveal, Defendant has made false and misleading explicit and implicit representations to potential customers, and others that Defendant's Signatera offers superior performance compared to Reveal.

ANSWER: Natera denies the allegations in Paragraph 76 of the Complaint.

77. Defendant's false and misleading statements and omission of relevant facts are likely to cause and have caused confusion, mistake, or deception about the nature, characteristics and qualities of Defendant's Signatera in comparison, connection, or association with Plaintiffs Reveal.

ANSWER: Natera denies the allegations in Paragraph 77 of the Complaint.

78. Defendant knows, or in the exercise of reasonable discretion should know, that its marketing program deceives potential customers about the nature, characteristics, and qualities of Signatera in comparison, connection, or association with Plaintiffs Reveal.

ANSWER: Natera denies the allegations in Paragraph 78 of the Complaint.

79. Defendant's conduct amounts to deception, trickery, and/or unfair methods and has damaged and jeopardized Plaintiffs business. As a result of such malicious, wanton, and/or fraudulent conduct, Defendant has caused, and unless enjoined by the Court, will continue to cause confusion as to the performance of Signatera in comparison to Plaintiffs Reveal.

ANSWER: Natera denies the allegations in Paragraph 79 of the Complaint.

80. Plaintiff is entitled to damages for Defendant's unfair competition, an accounting of profits made on sales of Defendant's product, and recovery of Plaintiff s costs of this action. Defendant's actions have been willful and have been undertaken with the purpose of deceiving consumers. Thus, Plaintiff is entitled to an award of punitive damages.

ANSWER: The allegations in Paragraph 80 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. To the extent an answer is required, Natera denies the allegations in Paragraph 80 of the Complaint. Natera specifically denies that Guardant is entitled to damages, an accounting of profits allegedly made on sales of Natera's product, recovery of costs of this action, punitive damages, or any other relief.

81. As a result of Defendant's conduct, Plaintiff has suffered, and unless such acts and practices are enjoined by this Court, will continue to suffer, damage to its business, reputation, and goodwill for which it is entitled to relief.

ANSWER: The allegations in Paragraph 81 of the Complaint state legal conclusions that Natera is neither required to admit nor deny. To the extent an answer is required, Natera denies the allegations in Paragraph 81 of the Complaint. Natera specifically denies that Guardant is entitled to any relief.

PRAYER FOR RELIEF

Natera denies that Guardant has any valid claim and denies that Guardant is entitled to any of the relief requested in its Prayer for Relief.

AFFIRMATIVE DEFENSES

Without conceding that it bears the burden of proof or persuasion as to any of the issues raised in these defenses (whether denominated as affirmative defenses or otherwise), as separate and distinct affirmative defenses to Guardant's Complaint, Natera alleges as follows:

FIRST AFFIRMATIVE DEFENSE

The Complaint, in whole or in part, fails to state a claim against Natera upon which relief can be granted.

SECOND AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, because Guardant lacks standing to sue.

THIRD AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, because the statements alleged therein concern matters of which there is legitimate ongoing scientific disagreement and are therefore not actionable.

FOURTH AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, by the doctrine of unclean hands.

FIFTH AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, by the doctrine of estoppel.

SIXTH AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, because Guardant cannot show that it will suffer irreparable harm.

SEVENTH AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, because Guardant has suffered no injury or damages.

EIGHTH AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, because to the extent Guardant suffered any damages, which Natera denies, Guardant failed to mitigate its damages.

NINTH AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, because to the extent Guardant suffered any injury or damages, which Natera denies, such injury or damages were not caused, proximately or otherwise, by any action of Natera.

TENTH AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, because Guardant's alleged injuries and

damages, if any, were proximately caused by the actions, inactions, and/or omissions of Guardant.

ELEVENTH AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, because any acts, conduct, and/or omissions alleged arise from a reasonable exercise of business judgment.

TWELFTH AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, because Guardant has an adequate remedy at law for any claims to equitable or injunctive relief.

THIRTEENTH AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, because the alleged speech complained of by Guardant is protected under the First Amendment.

FOURTEENTH AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, because Guardant has waived whatever rights it may otherwise have had to bring its causes of action.

FIFTEENTH AFFIRMATIVE DEFENSE

The Complaint may be barred, in whole or in part, because Guardant would be unjustly enriched if allowed to recover any portion of the damages alleged in the Complaint.

SIXTEENTH AFFIRMATIVE DEFENSE

The Complaint contains insufficient information to permit Natera to raise all appropriate defenses, and therefore, Natera reserves the right to amend and/or supplement these defenses and to assert additional defenses.

RESERVATION OF DEFENSES

Additional defenses may be disclosed by discovery or additional factual allegations made by Guardant. Accordingly, Natera reserves the right to amend, modify, revise, or supplement its Answer, or to plead such further defense and/or take such further actions that may be necessary and proper to preserve such additional defenses.

COUNTERCLAIMS

In accordance with Rule 13 of the Federal Rules of Civil Procedure, Counterclaim-Plaintiff Natera, Inc. ("Natera") hereby alleged and asserts the following counterclaims against Counterclaim-Defendant Guardant Health, Inc. ("Guardant").

SUMMARY OF THE ACTION

1. Natera is a leader in non-invasive genetic testing. In August of 2017, Natera launched Signatera(TM), a novel personalized approach to cancer detection in plasma. The technology analyzes whole-exome sequencing data from a patient's tumor sample in order to custom design individual-specific assays, targeting mutations known to be present in the patient's tumor tissue ("tumor signatures"). This uniquely personalized "tumor informed" approach enables physicians to accurately detect and monitor cell-free tumor DNA ("ctDNA"). The Signatera test has been shown to detect the presence of ctDNA earlier than traditional tools, and with fewer false positives.

2. Detecting and monitoring ctDNA in the blood of a cancer patient allows physicians to detect minimal/molecular residual disease ("MRD") and recurrence of a patient's cancer. Detection of residual disease can lead to better patient outcomes by informing clinical decisions, including whether to treat with chemotherapy after surgery, whether to biopsy a suspicious lesion, or whether to continue or discontinue a particular treatment strategy.

3. This case arises from Guardant's campaign of false and misleading commercial statements regarding the performance of its purportedly competitive MRD product, "Reveal."[8]

4. Reveal is a "tumor-naive test," which means that it looks for evidence of alterations in the same genomic regions for every patient without accounting for the mutational signature of the specific patient's particular tumor.

5. Guardant supported and co-authored a study (the "Study") that it grossly mischaracterized and misrepresented in order to enhance the performance claims for its test. *See* Ex. A. Guardant then disseminated these false and misleading claims regarding the effectiveness of its test to influence healthcare professionals and patients to choose it over other MRD testing

[8] Guardant has previously referred to this test as its "Lunar-1" test.

products, such as Natera's product, Signatera. Such misinformation regarding the efficacy of the test not only put competitors such as Natera at a competitive disadvantage but also endangered the health and safety of patients who rely on MRD testing for important clinical decisions.

6. The Study is so narrow, its approach so flawed, and its data so limited that it cannot possibly support Guardant's broad performance claims.

7. Even prior to the publication of the Study, Guardant began spreading false and misleading information, allegedly based on the Study, to drive market share away from competitors such as Natera. Guardant's false and misleading statements about the performance of its MRD test have caused and—unless enjoined—will continue to cause significant injury to Natera, and potentially to cancer patients.

8. Guardant's actions violate Section 43(a) of the Lanham Act and amount to unfair competition, false advertising, and unfair business practices. Natera seeks monetary and injunctive relief based on Guardant's unlawful conduct.

THE COUNTERCLAIM PARTIES

9. Natera is a corporation organized and existing under the laws of the State of Delaware and has its principal place of business at 201 Industrial Rd., San Carlos, California 94070. Natera is a global leader in cell-free DNA testing. Natera's mission is to improve disease management around the globe, with a focus on women's health, oncology, and organ health.

10. Guardant is a corporation organized and existing under the laws of the State of Delaware and has its principal place of business at 505 Penobscot Dr., Redwood City, California 94063. Guardant may be served with process via its registered agent, CT Corporation System, 818 West Seventh Street, Suite 930, Los Angeles, California 90017.

JURISDICTION AND VENUE

11. Natera's counterclaims arise under Section 43(a) of the Lanham Act, 15 U.S.C. § 1125(a), the Federal Declaratory Judgment Act, 28 U.S.C. §§ 2201–2202 *et seq*., Cal. Civ. Proc. Code § 1060 *et seq.*, Cal. Bus. & Prof. Code § 17500 et seq., Cal. Bus. & Prof. Code § 17200 et seq., and the common law of California and other states in which Guardant is conducting its activities. An actual controversy exists under the Declaratory Judgment Act because Guardant has

asserted and is asserting violations of Section 43(a) of the Lanham Act by Natera, and Natera denies those allegations.

12. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331, 1338, 2201, and 2202. This Court has supplemental jurisdiction over Natera's state law claims pursuant to 28 U.S.C. § 1367.

13. This Court has personal jurisdiction over Guardant because Guardant has purposefully availed itself of the rights and privileges of this forum by virtue of the filing of its Complaint in this Court in Case No. 3:21-cv-04062-EMC on May 27, 2021. Guardant is also subject to specific personal jurisdiction in this District because it maintains a regular place of business in the District, and because, as set forth in detail below, acts giving rise to Natera's counterclaims have occurred in the Northern District of California, including disseminating false and misleading advertisements to physicians, patients, healthcare professionals, and others residing in California.

14. Venue is proper in this District as to these counterclaims pursuant to 28 U.S.C. § 1391 because, *inter alia*, Guardant has submitted to the venue of this Court by filing its complaint here. Venue is also proper because a substantial part of the events giving rise to Natera's counterclaims occurred and are continuing to occur in this District.

FACTUAL ALLEGATIONS

A. *Natera Launches Signatera.*

15. On August 21, 2017, Natera launched Signatera, a bespoke ctDNA test designed to detect and measure MRD in patients previously diagnosed with cancer, to aid detection of cancer recurrence. Signatera is able to detect MRD earlier than traditional methods, and thereby helps optimize treatment decisions. The test is available for both clinical and research use and has been granted three Breakthrough Device Designations by the Food and Drug Administration ("FDA") for multiple cancer types and indications. Signatera's performance has been clinically validated in multiple cancer types including colorectal, non-small cell lung, breast, and bladder cancers.

B. *Guardant Launches Reveal, a Tumor-Naïve MRD Test.*

16. On or around February 16, 2021, Guardant released a "tumor-naïve" MRD test, called Reveal. Like Signatera, Reveal is a ctDNA test, designed to detect the presence of MRD in

patients who have been previously diagnosed with cancer. Reveal is only validated for use in colorectal cancer, and has not been granted FDA Breakthrough Device Designation.

17. Guardant supported and co-authored the Study on the performance characteristics of Reveal, which was published on April 29, 2021. As explained in greater detail below, the Study's limited data, flawed methodology, and narrow focus cannot support Guardant's broad, inaccurate, and misleading performance claims. Although Guardant's marketing relies on the Study, the design of the Study and the data generated make these performance claims unsupported, unwarranted, and worse, unreliable.

C. *Measuring Performance of a ctDNA Test.*

18. Researchers generally evaluate the performance of a ctDNA test like Signatera or Reveal using two key metrics: sensitivity and specificity. Additional metrics relevant to the assessment of MRD performance are positive predictive value ("PPV"), negative predictive value ("NPV"), diagnostic lead time (the time between first MRD detection and confirmed radiographic recurrence), outcomes analysis, and hazard ratios ("HR").

19. Sensitivity measures the percentage of positive results that are correctly identified. A test with high sensitivity is more likely to correctly identify the presence of cancer in a blood sample in which MRD is in fact present, as verified by a clinical "gold standard," including that the patient subsequently experienced clinical or radiographic recurrence.

20. Specificity measures the percentage of negative results that are correctly identified. A test with high specificity is more likely to correctly identify the absence of cancer in a blood sample when no MRD is in fact present, as verified by a clinical "gold standard," including that the patient remains relapse-free or progression-free.

21. In order to be accurate and meaningful, sensitivity and specificity must be calculated and reported together in the same analysis of the same set of samples. Sensitivity and specificity cannot be interpreted by themselves, because those values can differ from analysis to analysis, based on several factors, including differences in patient cohort.

22. As explained in greater detail below, Guardant's marketing claims fundamentally misrepresent the data and conclusions of the Study to either obfuscate or artificially boost the above metrics and other performance data for the test.

D. *The Study Does Not Support Guardant's Marketing Claims.*

23. The Study's data and analysis fail to support Guardant's marketing claims in at least four fundamental ways: (1) the Study reported two different metrics for serial test performance: "longitudinal" and "surveillance," the latter metric having no legitimate clinical basis or scientific significance; (2) the Study does not include key metrics in its "surveillance" analysis, rendering Guardant's marketing claims into at best misleading half-truths; (3) the data was generated in a population that is not representative of Guardant's intended use for its test, such that Guardant's marketing claims reflect artificially elevated or unsupported metrics; and (4) Guardant's performance claims exclude data from the Study, which, if included, would substantially detract from those claims.

i. Guardant's Use of "Surveillance" Analysis Makes Guardant's Sensitivity Claims Misleading.

24. The Study reported two different metrics for serial test performance: "longitudinal" and "surveillance" metrics. These metrics refer to different points in time at which the researchers collect blood samples from patients following the initial (landmark) blood draw. Longitudinal analysis is typically limited to patients with any subsequent blood draw after the initial timepoint; no matter how much time has passed following the initial blood draw. Researchers frequently use longitudinal analyses because they offer significant real-world clinical value, similar to other blood-based biomarkers such as CEA (Carcinoembryonic Antigen).

25. Under a longitudinal analysis, the Study reported a sensitivity score of 69% and specificity score of 100%. The specificity score, however, facially indicating a false positive rate of zero, was only possible with the exclusion of two patients from the sample set, as explained in more detail below. In touting its Study to healthcare providers and cancer patients, Guardant deliberately omitted mentioning this critical exclusion.

26. The Study engaged in what it called a "surveillance" analysis, which, unlike longitudinal analysis, is not supported by medical or academic literature. Only under this unusual and unsupported analysis did the Study report a favorable sensitivity score. The Study defined a "surveillance" draw as a blood sample obtained within four months of clinical recurrence. The Study offered no scientific explanation or support for its arbitrary four-month cut-off date, except for a false attribution of this methodology to a study by Reinert et al, which in fact employed no such cutoff. Under the "surveillance" analysis employed for the Study, the authors reported a sensitivity metric of 91%, but no specificity metric.

27. Guardant's marketing claims of 91% in the "surveillance" context are derived from the particular and peculiar definition of "surveillance" in the Study, but Guardant intends for physicians and patients to confuse the Study definition with the commonly understood plain meaning of the term surveillance, *i.e.*, time points or time periods after completion of definitive treatments, including for example follow up testing when there are no signs of cancer after treatment.

28. Guardant's marketing claims deliberately confound the Study's peculiar definition of "surveillance" with "monitoring." In one presentation, Guardant's CEO describes surveillance as "multiple shots on goal," but this is *contrary* and in stark contrast to the definition of "surveillance" used in the Study—a single "shot on goal" within a four-month time period of recurrence.

ii. Guardant's Reliance on "Surveillance" Analysis Misleadingly Masks the Absence of Specificity Data.

29. Importantly, the Study did not report the corresponding specificity metric for the surveillance analysis. It is extremely unusual and misleading for a laboratory like Guardant to make marketing claims about their test using a sensitivity metric without presenting the corresponding specificity metric, as doing so makes it virtually impossible to draw any meaningful conclusions about a test's performance in that setting. Most scientists would consider a test invalid if both sensitivity and specificity cannot be evaluated together, as is the common and accepted practice.

30. Indeed, presenting sensitivity without the corresponding specificity is contrary to guidance from the FDA, Clinical Laboratory Improvement Amendments ("CLIA"), and the New York State Department of Health ("NYSDOH").

31. A test with a high sensitivity metric could have a low specificity rate; if a laboratory issued a positive test report for every patient without performing any testing at all, it would have a 100% sensitivity score. However, that test would have a very low specificity score, because it would have missed every true negative patient. The real-world consequences of such a defective test—individual patients being misinformed that they have tested positive for MRD—cannot be overstated. Such false positives may cause a patient to undergo unnecessary biopsies, surgeries, chemotherapy, radiation treatment, or other invasive and damaging procedures; result in emotional trauma to the patient and her loved ones; and needlessly waste time and other resources on expensive medical care.

32. A specificity score could not be meaningfully determined by utilizing the Study's unusual and unsupported "surveillance" method, because by definition, all patients in the sample group had experienced a recurrence of cancer, and it would be impossible to obtain a false positive within such a group.

33. Because the Study's authors did not determine or report the specificity measure for the surveillance analysis, the Study fails to rule out the possibility that the test generates excessive false-positives. The intentional omission of this key metric not only renders the study materially flawed, it is also highly suspicious and deeply troubling. Because of Guardant's false and misleading marketing, patients and physicians are under the false impression that the test has a high specificity in the surveillance setting, when in fact they have no way of knowing whether this is true. Such misinformation disseminated to the oncology community risks serious adverse outcomes for patients.

34. The Study cannot support Guardant's marketing claims, because the Study analyzed "longitudinal" and "surveillance" samples only in patients who experienced recurrence, rather than a representative sample of patients. In other words, the Study only suggests how well the test could detect the presence of cancer, without claiming to determine how well the test was able to detect the absence of cancer. This makes it impossible to calculate specificity and renders Guardant's specificity claims in its marketing unsupported, if not irresponsible.

35. The Study evaluated "longitudinal" and "surveillance" draws only in patients who had experienced recurrence, so it has limited clinical value given the critical need for physicians and patients to know if cancer is present. Guardant's marketing materials exploit and abuse the Study's limited scope (i.e., its exclusive limitation to patients who had experienced recurrence). Guardant's marketing materials present an artificially high sensitivity score of 91% without reporting a corresponding specificity score in its "surveillance analysis."

36. In the Discussion section of the Study, the authors state, "the lack of systematic longitudinal and surveillance draws across all patients precluded a comprehensive assessment."

37. Guardant's marketing materials pair its unsupported 91% sensitivity score with a 100% specificity claim from a different analysis. *See, e.g.*, Ex. B at 17. Presenting sensitivity and specificity scores from different analyses together is extremely misleading, given the relationship between sensitivity and specificity. Of all of Guardant's false and misleading representations, this may be the most egregious. Guardant was forced to combine disparate data because of the aforementioned flaws in the Study.

38. The Study also omits results that would contradict Guardant's marketing claims. Specifically, the Study reported a specificity score from the longitudinal analysis of 100% in patients with at least one-year minimum clinical follow-up. However, the Study excluded the results from two patients whose test results would have negatively affected this specificity score. The Study excluded these patients' results because the patients had not had at least one year minimum clinical follow up; however there was no justification offered for the one-year cutoff, especially in the context of the mis-aligned four-month cutoff described earlier and the average diagnostic lead time observed in the Study of approximately four months. Furthermore, the Study was initiated more than a year ago, and Guardant (as both a co-author of the Study and provider of testing) has had ample opportunity to follow up with the two patients well in advance of the Study's publication, issue supplemental findings, and update their marketing materials accordingly. Guardant evidently chose to ignore this additional data in its marketing claims. The plausible inference to be drawn is that Guardant has excluded unfavorable results from its marketing claims to enable its alleged specificity claim of 100%.

39. There is another issue with the Study's calculation of "longitudinal" specificity. For the "longitudinal" analysis, the Study stated that "longitudinal time points were defined by patients who had subsequent draws to the landmark timepoint." The problem is that the only patients in the Study with a blood draw subsequent to the landmark timepoint were those for whom there was a recurrence. In other words, due to the makeup of the Study cohort, the only data points in the longitudinal specificity analysis were from the affected population. Because specificity is a measure of the test's ability to correctly identify a negative result, and because there were no unaffected patients in the cohort for the test to identify, the longitudinal specificity of the test, based on the Study data, is not 100%, but rather completely unknown. Guardant's marketing claims referencing a 100% longitudinal specificity are therefore inherently false and misleading.

40. Moreover, the Study appears to lack many of the parameters necessary to support Guardant's marketing claims. For instance, the Study appears to have evolved significantly over time, and there is no indication that there were any predefined serial blood draw schedules, or predefined endpoints. In short, the Study is missing the necessary indicia of a reliable validation, and it is deeply misleading for Guardant to use it as the basis for its false and sweeping marketing claims.

E. ***Guardant Disseminates False and Misleading Information.***

i. Guardant Misrepresents Reveal's Performance Characteristics Compared to CEA.

41. Guardant's claims concerning the test in comparison to CEA (Carcinoembryonic Antigen) are misleading, since a non-clinically established CEA cutoff was used in the analysis. In the Study, the test was compared to CEA in the "landmark" analysis. Despite claiming in a press release that "by detecting recurrence months earlier than current standard of care methods like carcinoembryonic antigen (CEA)" (Ex. C), the Study contains no analysis of the test's lead time as compared to CEA.

42. Furthermore, the Study's definition of abnormal CEA used a non-standard cutoff of 3.4 ng/mL. The references provided in the Study do not support using this cutoff, which has, to our knowledge, not been utilized in this setting. The clinical cutoff in most widespread use is 5 ng/mL,

(which is the cutoff used in prior ctDNA studies in the intended use population). Some have examined other cutoffs, but not 3.4.

ii. Guardant Misrepresents Reveal's Sensitivity Data.

43. On or around February 16, 2021, Guardant issued a press release, in which it made numerous false and misleading statements regarding the performance of its test. *See* Ex. C.

44. In the press release, Guardant claimed that its test had achieved an "industry leading" sensitivity measure of 91%. *Id.* This claim is demonstrably false. The only comparable performance data comes from the Study's "longitudinal" analysis, which reported a sensitivity measure of 69%. The test's sensitivity score of 69% is far from "industry leading"; multiple ctDNA tests on the market, including Natera's Signatera test, have achieved significantly higher sensitivity scores with longitudinal testing. Even this comparison is flawed, given that the Study's definition of "longitudinal" timepoints prevents a corresponding specificity from being calculated.

45. Guardant's claim that it achieved an "industry leading" sensitivity score of 91% is demonstrably false for two reasons: first, its test has not achieved a reliable sensitivity score of 91%, given its exclusion of cases in its landmark analysis; and second, its actual sensitivity score lags behind its competitors in the market, including Natera's Signatera test. This is in addition to the fact that it is inherently misleading to report sensitivity without corresponding specificity in the same patient population.

46. Guardant appears to have relied exclusively on the Study in support of its claimed 91% sensitivity rate. *See* Ex. A. As explained above, the Study reported the 91% sensitivity metric only for the scientifically invalid "surveillance analysis" without reporting other key metrics necessary to substantiate marketing claims about the test's purported sensitivity score and overall effectiveness. Therefore, the surveillance analysis cannot properly be relied upon as a measure of the test's performance. It also renders the Study materially and substantially flawed.

47. In short, the Study is not sufficient for Guardant to have concluded with any reasonable degree of certainty that it actually established either a sensitivity rate of 91% for the test or "industry leading" performance.

48. Guardant continues to flaunt and tout these misleading results. By way of example, in connection with the 2021 Annual Meeting of the American Society of Clinical Oncology ("ASCO") that took place between June 4 to June 8, 2021, Guardant again presented the unfounded results of the Study to physicians and patients and, once more, inappropriately and misleadingly compared the sensitivity of Signatera and Reveal to Natera's detriment. Ex. H.

49. In particular, during Guardant's formal presentation at ASCO, Jessica Kurata, PhD, a Guardant Senior Bioinformatics Scientist, stated that "plasma-only MRD detection [i.e., Reveal] demonstrates favorable sensitivity and specificity for recurrence comparable to tissue dependent approaches [i.e., Signatera]." Ex. I. The accompanying PowerPoint presentation directly compared the sensitivity of tissue-naïve and tissue-dependent assays despite the lack of any reliable data that would support such a comparison. *See* Ex. H.

50. Guardant repeated these misleading representations to an audience of customers and potential customers despite being well aware of Natera's concerns regarding the results and reliability of the Study. In making these statements to the public in connection with its ASCO presentation, Guardant knew, and had every reason to know, the statements to be false and misleading.

iii. Guardant's "Industry Leading Performance" Claims Are False and Misleading.

51. Not only is Guardant's claim that its 91% sensitivity is "industry leading" false, but its more general claims of "industry leading performance" are also false. For example, its test has a pre-surgical detection rate of only 47% (Ex. A), compared to a pre-surgical detection rate of 89-94% for Natera's Signatera test. Ex. D. Guardant's test has a diagnostic lead time of approximately four months (*see* Ex. E and Ex. F, at 13) as compared to a diagnostic lead time of 8.7 months for Natera's Signatera test (*see* Ex. D). A test that lags at least one competitor by such significant margins in such important performance metrics cannot truthfully call its performance "industry leading."

52. Pre-surgical detection rate and diagnostic lead time are industry-standard metrics for the evaluation of MRD test performance. Guardant concedes the importance of pre-surgical test performance in its prior validation studies using pre-surgical samples to establish assay performance

metrics, such as its claim in press releases and investor presentations of "reportable range down to 0.01 percent" (a claim unsupported by peer reviewed data). Guardant's consistent failure to report these metrics from the Study and include them in its comparative claims render those claims false and misleading.

iv. Guardant Makes False and Misleading Claims About the Analytical Performance of Reveal.

53. In its February 16, 2021 press release, Guardant claimed "the test accurately reports genomic alterations down to allele frequencies of 0.01 percent." Ex. C. There is no published peer-reviewed evidence to support this claim.

v. Guardant Cherry Picks Data.

54. Guardant made additional misrepresentations during a presentation at the January 11, 2021 JPMorgan Health Conference, which was disseminated to healthcare professionals, investors, potential patients, and others throughout the United States.

55. Recognizing the critical importance of reporting both the sensitivity and specificity rate, Guardant cherry-picked sensitivity metrics from one analysis and specificity metrics from a separate analysis. Specifically, Guardant claimed that the test had achieved a sensitivity metric of 91%—a figure derived from the Study's medically and scientifically unsupported "*surveillance*" analysis—and a specificity metric of 100%—a figure derived from either the Study's "*longitudinal*" or "landmark" analysis, and only after excluding the two false positive cases as described above. *See* Ex. B at 17. Guardant presented these metrics together with each other, giving the clear, but false, impression that they were reported in the same analysis, when in fact they were not. Guardant intentionally misled healthcare professionals and investors into believing that they could rely upon this data to evaluate the test's effectiveness.

56. Guardant's decision to commercially promote a sensitivity metric paired with a specificity metric from a different analysis was intentionally designed to mislead about the test being more effective than it actually is and superior to other products on the market, including Signatera. Such misinformation regarding the relative accuracy of competing oncological diagnostic products puts patients at unnecessary risk and creates waste and inefficiency in healthcare.

vi. Guardant's Claims Are Not Applicable to the Intended Use Population.

57. Guardant has made false and misleading statements regarding the test's effectiveness in other public communications.

58. In a press release posted to its website, Guardant claimed, "For oncologists, the test improves the management of *early-stage* CRC [colorectal cancer] patients by detecting ctDNA in blood after surgery to identify patients with residual disease who may benefit most from adjuvant therapy." Ex. G (emphasis added). However, the Study upon which Guardant relies for this claim contained at least 19% Stage-IV CRC patients who do not qualify as "early-stage" CRC patients. Guardant fails to account for the impact the significant percentage of Stage-IV patients would have on the results of the Study. Moreover, Guardant failed to identify the number of recurrences that were driven by the Stage IV group. Accordingly, Guardant's claim that the test improves the management of early-stage CRC patients is highly misleading.

59. One of the authors of the Study acknowledged this limitation, stating "I think one of the limitations that we discussed in our paper was this is not a pure population of only stage II or III. It is a mix of all four stages." Molika Ashford, *Guardant MRD Test Performs Well in Small Study as Tissue-Informed Debate Takes Shape*, PRECISION ONCOLOGY NEWS (May 7, 2021), https://www.precisiononcologynews.com/liquid-biopsy/guardant-mrd-test-performs-well-small-study-tissue-informed-debate-takes-shape#.YLE36ahKj-g.

60. Guardant's claim that Reveal can "identify patients with residual disease who may benefit most from adjuvant therapy" (Ex. G) is misleading for the additional reason that there is insufficient evidence that Reveal is in fact applicable to post-surgical adjuvant treatment decisions. No performance data has been presented using plasma samples taken in the first two-to-six weeks post-surgery, which is the critical window of time for a physician to decide whether to recommend adjuvant chemotherapy.

61. Many patients in the Study received neoadjuvant therapy, which is chemotherapy and/or radiotherapy prior to surgery. Such treatment may limit eligibility for further adjuvant treatment per established clinical guidelines. Therefore, these patients may not be considered part of the intended-use population.

F. *Guardant Disseminated Its False Claims Through Interstate Commerce.*

62. Guardant disseminated false and misleading statements regarding the effectiveness of Reveal in interstate commerce. Both the February 16, 2021 press release (Ex. C), and the undated publication discussed in Paragraphs 58 and 60, above (Ex. G) were posted on Guardant's website and transmitted throughout the world. Additionally, the false statements Guardant made during the JPMorgan Healthcare Conference (*see* Ex. B) were made via video- and telephone conference to healthcare professionals, investors, potential patients, and other participants throughout the United States, and the presentation deck containing the misrepresentation has since been circulated to persons throughout the United States.

G. *Guardant's False and Misleading Statements Were Made in the Context of Commercial Marketing, Advertising and/or Promotion.*

63. Guardant made the false and misleading statements detailed above in the context of commercial marketing, advertising, and/or promotion. For example, Guardant's February 16, 2021 press release was to publicly announce the commercial release and availability of the Reveal assay. Ex. C ("Guardant Health Launches Guardant Reveal™ Liquid Biopsy Test for Residual Disease and Recurrence Monitoring in Patients with Early-Stage Colorectal Cancer"). As another example, a month earlier, Guardant's January 11, 2021 presentation at the JPMorgan Healthcare Conference showed the Reveal packaging and previewed the product's commercial launch of Reveal. Ex. B at slide 19 ("Launching in Q1 2021"), 33 ("Launching Guardant Reveal for use in early-stage colorectral cancer").

64. Each of the false and misleading statements recounted above were widely circulated to decision makers, including healthcare professionals, investors, and others in order to influence those decision makers to recommend, use, purchase, or otherwise choose the test over competing—and even superior—products. Guardant intended its statements about alleged performance benefits to be heard loud and clear by potential customers and for them to choose Reveal over other competing products, including Signatera.

H. *Guardant's False and Misleading Statements Were Material.*

65. Guardant's false and misleading statements were material. These statements misrepresented the overall effectiveness of the Reveal test—an inherent characteristic of the Reveal test and a critical consideration for any decision maker in deciding whether to prescribe, use, or otherwise choose the test over a different diagnostic product, such as Signatera. Each of the statements was intended to, and likely did influence decision makers, including healthcare professionals, investors, and others to choose the test over other products, such as Signatera, that have been thoroughly validated, with evidence of effectiveness and performance better than Reveal.

66. Guardant knowingly and willfully communicated these statements to the public, including the potential customers of both Signatera and Reveal.

I. *Guardant's False and Misleading Statements Have Caused and Will Continue to Cause Natera to Suffer Significant Harm.*

67. Guardant continuously and knowingly provided false and misleading information to healthcare professionals and the public in order to drive business away from its competitors, such as Natera, to purchase Guardant's Reveal test. *See, e.g.*, *supra* ¶¶ **Error! Reference source not found.**-50.

68. As a result of Guardant's false and misleading statements, Natera has suffered—and, absent relief from this Court, will likely continue to suffer—significant harm, including lost revenue, loss of goodwill, and diminished reputation.

CLAIMS FOR RELIEF

COUNT I

Violation of Section 43(a) of the Lanham Act, 15 U.S.C. § 1125(a) by Guardant

69. Natera incorporates by reference all allegations set forth above as if fully set forth herein.

70. Guardant made false and misleading statements, including but not limited to press releases, at least one public presentation, and written promotional materials to healthcare professionals, insurance providers, patients, members of the public, and others, about the performance and quality of its Reveal tests. Guardant's false and misleading statements are designed

to—and likely will continue to—mislead healthcare professionals, patients, and others into believing that the Reveal test performs better than it actually does, and that it is superior to Natera's Signatera. Guardant's statements are literally false and/or are misleading commercial speech in violation of the Section 43(a) of the Lanham Act, 15 U.S.C. § 1125(a).

71. Guardant made these false and misleading statements in interstate commerce, and in the context of commercial advertising or promotion as they were made for the purpose of influencing healthcare providers, patients, and others to recommend, use, purchase, and otherwise prefer the Reveal test over competing and even superior products, such as Natera's Signatera.

72. Guardant intended for these false and misleading statements to deceive healthcare providers, patients, and others about the quality and performance of its test.

73. Guardant's false and misleading statements are material and likely will influence the decisions of healthcare providers, patients, and others.

74. Guardant's false and misleading statements are material and likely will influence healthcare providers, patients, and the general public to choose the test over Signatera.

75. Guardant made these false and misleading statements knowingly and willfully.

76. Natera has suffered—and will likely continue to suffer—significant harm as a result of Guardant's false and misleading statements, including lost revenue and loss of goodwill and diminished reputation.

77. Guardant's conduct constitutes false and misleading statements about its own goods and services and a competitor's goods and services in violation of Section 43(a) of the Lanham Act. Natera is therefore entitled to all relief available under Section 1117(a) of the Lanham Act, including but not limited to disgorgement of Guardant's profits, actual damages, and attorneys' fees and costs.

78. Further, and unless enjoined by this Court, Guardant's acts will irreparably injure Natera's goodwill and erode its market share, for which Natera has no adequate remedy at law. Pursuant to 15 U.S.C. § 1116, Natera is entitled to preliminary and permanent injunctive relief to prevent Guardant's continuing acts.

COUNT II

False Advertising in Violation of Cal. Bus. & Prof. Code § 17500 et seq. by Guardant

79. Natera incorporates by reference all allegations set forth above as if fully set forth herein.

80. Natera brings this counterclaim pursuant to Cal. Bus. & Pro. Code § 17535 in an individual capacity and not on behalf of the general public.

81. Cal. Bus. & Prof. Code § 17500 provides that it is unlawful for any person, firm, corporation or association to dispose of property or to perform services, or anything of any nature whatsoever or to induce the public to enter into any obligation relating thereto, to make or disseminate before the public, through the use of untrue and misleading statements that were known, or should have been known with the exercise of reasonable care, to be untrue and misleading.

82. Cal. Bus. & Prof. Code § 17508 provides, in pertaining part, "(a) it shall be unlawful for any person doing business in California and advertising to consumers in California to make any false or misleading advertising claim, including claims that (1) purport to be based on factual, objective, or clinical evidence, (2) compare the product's effectiveness or safety to that of other brands or products, or (3) purport to be based on any fact."

83. Guardant has violated Cal. Bus. & Prof. Code §§ 17500 and 17508 by making untrue and misleading statements, including but not limited to press releases, at least one public presentation, and written promotional materials to healthcare professionals, insurance providers, patients, and others, about the performance and quality of its Reveal test. Guardant's untrue and misleading statements are designed to—and likely will continue to—mislead healthcare professionals, patients, and others into believing that the Reveal test performs better than it actually does, and that it is superior to Natera's Signatera.

84. Guardant's false and misleading statements purport (but fail) to be based on factual, objective, or clinical evidence. The false and misleading statements improperly compare Guardant's Reveal test to Natera's Signatera where (to date) no appropriate head-to-head study has been performed, and those comparative statements likely will influence healthcare providers, patients, and the general public to choose Guardant's Reveal test over Signatera. Guardant's false and

misleading statements further purport (but fail) to be based on facts; in truth they are distortions of fact and context-bereft statements that are false or wholly misleading.

85. Guardant made these false and misleading statements knowingly and willfully.

86. As result of Guardant's violations, Natera has suffered—and, unless Guardant's conduct is enjoined by this Court, will likely continue to suffer—irreparable injury, including, but not limited to, the loss of revenue, goodwill, and diminished reputation.

87. Guardant's conduct has caused Natera damage in an amount to be determined at trial. Natera is entitled to damages to compensate for all actual harm caused by Guardant's conduct.

88. Pursuant to Cal. Bus. & Prof. Code § 17535, Natera seeks an order of this Court (1) compelling Guardant to provide restitution, and to disgorge monies to which Natera is entitled but were instead collected and realized by Guardant as a result of its false and misleading statements, and (2) providing injunctive relief enjoining Guardant from making such false and misleading statements.

COUNT III

Unlawful Trade Practice in Violation of Cal. Bus. & Prof. Code § 17200 et seq. by Guardant

89. Natera incorporates by reference all allegations set forth above as if fully set forth herein.

90. Under Cal. Bus. & Prof. Code § 17200, unfair competition is defined as and includes any unlawful, unfair, or fraudulent business act or practice and unfair, deceptive, untrue or misleading advertising. This includes, but is not limited to, any conduct or statement related to the operation of a business that is deceptive, untrue, misleading, and/or fraudulent.

91. Guardant has violated Cal. Bus. & Prof. Code § 17200 by making untrue and misleading statements, including but not limited to press releases, at least one public presentation, and written promotional materials to healthcare professionals, insurance providers, patients, and others, about the performance and quality of its Reveal test. Further, Guardant's conduct constitutes a violation of the Lanham Act, and thus its unlawful business conduct is separately actionable as a violation of Cal. Bus. & Prof. Code § 17200 *et seq*. Guardant's conduct is also independently unlawful and unfair, in violation of these provisions.

92. As result of Guardant's violation, Natera has suffered—and, unless Guardant's conducts are enjoined by this Court, will likely continue to suffer—irreparable injury, including, but not limited to, goodwill and diminished reputation for which Natera has no adequate remedy at law.

93. Guardant's conduct has caused Natera damage in an amount to be determined at trial. Natera is entitled to damages to compensate for all actual harm caused by Guardant's conduct.

94. Guardant has been unjustly enriched from its conduct. Pursuant to Cal. Bus. & Prof. Code § 17203, Natera seeks an order of this Court compelling Guardant to provide restitution, and to disgorge monies to which Natera is entitled but were instead collected and realized by Guardant as a result of its false and misleading statements and injunctive relief enjoining Guardant from making such false and misleading statements.

95. Natera is further entitled to recover costs and attorneys' fees pursuant to California Unfair Competition Law.

COUNT IV

Common Law Unfair Competition by Guardant

96. Natera incorporates by reference all allegations set forth above as if fully set forth herein.

97. Guardant made false and misleading statements, including but not limited to press releases, at least one public presentation, and written promotional materials to healthcare professionals, insurance providers, patients, and others, about the performance and quality of its Reveal test compared to Natera's Signatera. Guardant's false and misleading statements are likely to cause and have caused confusion, mistake, or deception about the nature, characteristics and qualities of Guardant's Reveal in comparison, connection, or association with Natera's Signatera.

98. Guardant knows, or in the exercise of reasonable discretion should know, that its marketing program deceives healthcare providers, patients, and the general public about the nature, characteristics, and qualities of Reveal in comparison, connection, or association with Natera's Signatera

99. Guardant's conduct amounts to deception, trickery, and/or unfair methods and has damaged and jeopardized–and will likely continue to damage and jeopardize–Natera's business, including lost revenue and loss of goodwill and diminished reputation.

100. As a result of Guardant's malicious, wanton, and/or fraudulent conduct, Guardant has caused and will continue to cause confusion as to the performance of Reveal in comparison to Natera's Signatera. Guardant's conduct has caused Natera to suffer and, unless enjoined by the Court, will cause Natera to continue to suffer, irreparable harm to its business, reputation, and goodwill that cannot be adequately remedied at law and for which it is entitled to relief.

101. Natera is entitled to damages for Guardant's unfair competition, an accounting of profits made on sales of Guardant's product, and recovery of Natera's costs of this action.

102. Guardant's actions have been willful and have been undertaken with the purpose of deceiving consumers. Thus, Natera is entitled to an award of punitive damages.

COUNT V

Declaratory Judgment of No Lanham Act Violation by Natera

103. Natera incorporates by reference all allegations set forth above as if fully set forth herein.

104. Guardant's allegations that acts by Natera have violated Section 43(a) of the Lanham Act (as asserted in Guardant's complaint) have no basis in law or fact, and fail to state a claim for relief.

105. To resolve the legal and factual questions raised by Guardant and to afford relief from the uncertainty and controversy from which Guardant's accusations have precipitated, Natera is entitled to declaratory judgment that it does not violate Section 43(a) of the Lanham Act.

106. A judicial declaration pursuant to the Federal Declaratory Judgment Act (28 U.S.C. §§ 2201-2202 *et seq.*) concerning this matter is necessary and appropriate so that Natera can ascertain its belief that it can make commercial statements free from challenge that its actions violate the law.

COUNT VI

Declaratory Judgment of No False Advertising Under Cal. Bus. & Prof. Code § 17500 *et seq.* by Natera

107. Natera incorporates by reference all allegations set forth above as if fully set forth herein.

108. Guardant's allegations that acts by Natera have violated Cal. Bus. & Prof. Code § 17500 *et seq.* (as asserted in Guardant's complaint) have no basis in law or fact, and fail to state a claim for relief.

109. To resolve the legal and factual questions raised by Guardant and to afford relief from the uncertainty and controversy from which Guardant's accusations have precipitated, Natera is entitled to declaratory judgment that it does not violate Cal. Bus. & Prof. Code § 17500 *et seq.*

110. A judicial declaration pursuant to Cal. Civ. Proc. Code § 1060 *et seq.* concerning this matter is necessary and appropriate so that Natera can ascertain its belief that it can make commercial statements free from challenge that its actions violate the law.

COUNT VII

Declaratory Judgment of No Unlawful Trade Practice Under Cal. Bus. & Prof. Code § 17500 *et seq.* by Natera

111. Natera incorporates by reference all allegations set forth above as if fully set forth herein.

112. Guardant's allegations that acts by Natera have violated Cal. Bus. & Prof. Code § 17200 *et seq.* (as asserted in Guardant's complaint) have no basis in law or fact, and fail to state a claim for relief.

113. To resolve the legal and factual questions raised by Guardant and to afford relief from the uncertainty and controversy from which Guardant's accusations have precipitated, Natera is entitled to declaratory judgment that it does not violate Cal. Bus. & Prof. Code § 17200 *et seq.*

114. A judicial declaration pursuant to Cal. Civ. Proc. Code § 1060 *et seq.* concerning this matter is necessary and appropriate so that Natera can ascertain its belief that it can make commercial statements free from challenge that its actions violate the law.

COUNT VII

Declaratory Judgment of No Common Law Unfair Competition by Natera

115. Natera incorporates by reference all allegations set forth above as if fully set forth herein.

116. Guardant's allegations that acts by Natera give rise to common law unfair competition claims (as asserted in Guardant's complaint) have no basis in law or fact, and fail to state a claim for relief.

117. To resolve the legal and factual questions raised by Guardant and to afford relief from the uncertainty and controversy from which Guardant's accusations have precipitated, Natera is entitled to declaratory judgment that Guardant has no claim for common law unfair competition.

118. A judicial declaration pursuant to Cal. Civ. Proc. Code § 1060 *et seq.* concerning this matter is necessary and appropriate so that Natera can ascertain its belief that it can make commercial statements free from challenge that its actions violate the law.

PRAYER FOR RELIEF

WHEREFORE, Natera respectfully asks this Court to award the following relief:

1. Judgment in favor of Natera and against Guardant;

2. An Order that Natera has not violated Section 43(a) of the Lanham act, Cal. Bus. & Prof. Code § 17500 *et seq.*, Cal. Bus. & Prof. Code § 17200 *et seq.*;

3. An order that Guardant is not entitled to any relief for its allegations of common law unfair competition;

4. An Order preliminarily and permanently enjoining Guardant from disseminating or causing the dissemination of false and misleading statements regarding its products or Natera's products;

5. An Order declaring no Lanham Act violation by Natera;

6. An Order declaring no false advertising under Cal. Bus. & Prof. Code § 17500 *et seq.* by Natera;

7. An Order declaring no unlawful trade practices Cal. Bus. & Prof. Code § 17200 *et seq.* by Natera;

8. An Order declaring no common law unfair competition by Natera;

9. An Order requiring Guardant to publish corrective statements;

10. Natera's actual monetary damages, including but not limited to Natera's lost business and profits, harm to Natera's goodwill and reputation, as well as Guardant's ill-gotten and unjustly derived gains pursuant to 15 U.S.C. § 1117(a), Cal. Bus. & Prof. Code §§ 17200 et. seq. and 17500 et. seq., and the common law of the State of California;

11. Punitive and exemplary damages;

12. Pre- and post-judgment interest on all damages awarded, as permitted by law;

13. Costs associated with litigation, including expert witness fees, as permitted by law;

14. Attorneys' fees to the extent permitted by law;

15. Statutory damages as permitted by law;

16. Such other relief at law or in equity to which Natera is entitled.

DEMAND FOR JURY TRIAL

Pursuant to Rule 38 of the Federal Rules of Civil Procedure, Natera demands a trial by jury on all issues so triable.

DATED: June 22, 2021

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